Restriction Requirement

In the Office Action mailed May 1, 2007, a Requirement for Restriction against pending claims 1-28 was made, requiring election among:

Group I: **claims 1-17, 22 and 23** drawn to a combination of at least two antibodies comprising at least two different multivalent antibodies, an antigen binding domain specific to a tumor antigen, an antigen-binding domain specific to an antigen present on human T-cells, or an antigen-binding domain specific to an antigen present on CD3-epsilon negative human effector cells and a composition containing the combination of antibodies;

Group II: **claims 18-20 and 22,** drawn to a polynucleotide encoding a combination of at least two antibodies characterized by the properties of claim 1, an expression vector, and a host cell containing said expression vector;

Group III: **claim 21,** drawn to a process for the preparation of a combination of antibodies according to claim 1;

Group IV: **claims 24, 25 and 28,** drawn to a method for treating B-cell malignancies, B-cell mediated autoimmune disease or the depletion of B-cells, the method comprising administering a therapeutically effective amount of a composition;

Group V: **claims 26 and 27,** drawn to a gene therapy method for treating B-cell malignancies, B-cell mediated autoimmune diseases or the depletion of B-cells, the method comprising administering a therapeutically effective amount of the polynucleotides or expression vector.

Applicant elects, with traverse, Group I, consisting of claims 1-17, 22 and 23, drawn to a combination of at least two antibodies as set forth above, not classified in any class or subclass by the Office Action mailed May 1, 2007.

Traversal of Restriction

In order for a Restriction Requirement to be made, there must be independent or distinct inventions, which would provide a serious burden on the examiner if restriction is not required.

In listing the Groups, as set forth above, the examiner characterizes the claimed combinations as "...comprising at least two different multivalent antibodies, an antigen binding domain specific to a tumor antigen, an antigen-binding domain specific to an antigen present on human T-cells, or an antigen-binding domain specific to an antigen present on CD3-epsilon negative human effector cells..." Applicants hereby clarify that the combination of claim 1 comprises at least two antibodies, where both must be present: 1) a first antibody comprising an antigen binding domain specific to a tumor antigen and an antigen binding domain specific to an antigen present on CD3-episilon negative human effector cells and 2) a second antibody comprising an antigen binding domain specific to a tumor antigen and an antigen binding domain specific to an antigen present on human T-cells. In order to clarify this characteristic, applicants have amended claim 1 as set forth above.

Accordingly, the claims of the application are linked by a single inventive concept, wherein that single inventive concept is a combination of at least two antibodies, each antibody having the characteristics as described and claimed.

Species Election

The requirement for a species election is traversed. As set forth in MPEP §803, a proper restriction requirement is made when the inventions are independent (MPEP §§ 802.01, 806.04, 808.01) or distinct as claimed (MPEP §§ 806.05-806.05(i)); and there is a serious burden on the Examiner if restriction is not required (MPEP §§ 803.02, 806.04(a)-(i), 808.01(a) and 808.02). However, even if the species are viewed as independent or distinct, but the claimed subject matter in each group is related by a "commonality of operation, function and effect" (MPEP § 806.04(e)), then requiring election of a single species is improper. Additionally, MPEP § 803 states that "[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions."

It is stated in Item 2 of the Office Action mailed May 1, 2007 that "...[t]he claims further list two patentably distinct species of tumor antigen, three patentably distinct species of T cell antigens and four patentably distinct species of effector cell antigens." No further classification of the alleged species is provided. It is not immediately clear from the examiner's Office Action which claims the species are alleged to be recited in or exactly which species require election.

While claims 2-5 list tumor antigens, claim 6 lists T cell antigens and claim 7 lists effector cell antigens, the examiner (in Item 3) identifies only claims 6, 7, 14 and 15 as generic claims. It is believed that claim 1 should also be included in this list of generic claims. Also the subject matter of claims 14 (types of antibodies) and 15 (selective binding target) is not included in the examiner's list of species.

It is submitted that the species of the group identified as antigens in Items 2 and 3 of the Office Action mailed May 1, 2007 possess a commonality of design, operation or effect and therefore relate to a single general inventive concept. Specifically, each species is the target of an antigen binding domain on a combination of antibodies, as set forth in claim 1, where the combination contains at least two antibodies, and each antibody has at least two specificities. As all of these targets are targets of antigen binding domains on the antibodies, they satisfy the criterion of "commonality of design, operation or effect."

The species of the group identified as natural antibodies in claim 14 are all antibodies classified as "natural antibodies" As such the group possesses a "commonality of design, operation or effect."

The species of the group identified as binding targets in claim 15 are all targets to which an antibody of the claimed combination of antibodies can bind. As such the group possesses a "commonality of design, operation or effect."

In order that this response fairly meets the substance of the Office Action in all respects, even though the election requirement is traversed by Applicants, a single disclosed species of each group listed in Item 2 of the Office Action mailed May 1, 2007 is elected by applicants, with traverse: i) CD19 of the "two patentably distinct species of tumor antigen," as recited in claims 2 and 3; ii) CD3 of the "three patentably distinct species of T cell antigens," as recited in claim 6; iii) CD16 of the "four patentably distinct species of effector cell antigens," as recited in claims 7 and 8; iv) humanized antibody of the antibodies as recited in claim 14; and v) protein as the selected binding target as recited in claim 15.

It is acknowledged by applicants that in a species election, if any species is found to be allowable, then an additional species will be examined, until all species have been examined. *i.e.* all recited tumor antigens, all recited T cell antigens, all recited effector cell antigens, all recited antibodies and all recited binding targets. If any generic claim is finally held to be allowable, all

claims drawn to species containing all elements of the generic claim will also generally be held to be allowable. (MPEP § 806.04(d)).

Accordingly, it is respectfully requested that all species be retained in the aggregate for examination or, alternatively, that an additional explanation in support of a species election requirement be provided.

CONCLUSION

In response to the Requirement for Restriction dated July 31, 2006, Applicants have provisionally elected, with traverse, Group I, claims 1-17, 22, and 23 drawn to a combination of at least two antibodies. Further, Applicants have provisionally elected CD19, CD3, CD16, humanized antibodies and proteins of the dependent claims of Group I, as a single disclosed species, with traversal of the election of species requirement.

The time for responding to the May 1, 2007 Office Action without extension was set at one months, or June 1, 2007. Applicants hereby request a one month extension of time under 37 C.F.R. § 1.136 to extend the deadline for response to and including July 1, 2007. As July 1, 2007 was on a Sunday, the filing of the present response is therefore timely. Payment of the extension fee of $60.00 specified in 37 C.F.R. § 1.17(a)(1), as applicable to small entity, is authorized by the enclosed Credit Card Payment Form PTO-2038. Should any additional fees be required or an overpayment of fees made, please debit or credit our Deposit Account No. 08-3284, as necessary.

If any additional issues remain, the Examiner is requested to contact the undersigned attorney at (919)419-9350 to discuss same, in order that the prosecution of this application is expedited.

Respectfully submitted,

Date: July 2, 2007

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Enclosures:
Credit Card Form PTO-2038 [1 pg.]

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